

Primary rectal monophasic synovial sarcoma

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ABSTRACT

Synovial sarcoma is a rare malignant mesenchymal neoplasm that often occurs in the extremities. Less than 70 cases of primary synovial sarcoma occurring in the digestive system have been reported. We present a case of a 48-year-old woman with a spindle cell tumor in the rectum that stained positive for AE1/3 (focal), vimentin, CD99, BCL2, EMA (focal), and MiB-1 (15%). Ultimately, the lesion was diagnosed as a primary rectal monophasic synovial sarcoma and confirmed by molecular testing for SYT/SSX1 gene fusion. Analysis of previous publications indicated that patients of advanced age or a large tumor size (≥ 5 cm) have a higher risk of progressing rapidly to death after diagnosis of synovial sarcoma in the digestive system.

KEYWORDS Gastrointestinal tract; monophasic; rectum; synovial sarcoma; SYT/SSX1

Synovial sarcoma (SS) is a malignant mesenchymal neoplasm that accounts for 5.4% of soft tissue sarcomas and often occurs in the extremities.¹ Primary gastrointestinal SS is rare. To our knowledge, less than 70 cases (including four rectosigmoid colon cases) of SS arising from the esophagus, stomach, and intestine have been reported (*Table 1*).^{2–45} We present a case of primary SS arising from the rectum.

CASE PRESENTATION

A 48-year-old woman presented with intermittent rectal bleeding and was found to have a large exophytic rectal mass on colonoscopy. Her past medical history was noncontributory. Her social history included one to two alcoholic drinks daily for the past 20 years. Her family history was significant for a father who died of prostate cancer. On digital rectal exam, there was a palpable 4 to 5 cm broad-based mass that was freely movable, firm, and clinically extending into the submucosa.

Multiple biopsies were taken. Microscopic examination revealed high-grade neoplasm that had oval to spindled cells arranged in solid sheets with focal discohesive areas. The tumor cells were negative for CAM5.2, S100, CD10, CD34, CD117, muscle specific actin, smooth muscle actin, NSE, and desmin and positive for AE1/3 (focal), vimentin, CD99, BCL2, EMA (focal), and MiB-1 (15%). The case was sent

for molecular analysis at an outside institution to rule out the possibility of SS, due to the unusual location. A SYT/SSX1 fusion transcript was detected by real-time polymerase chain reaction, and a final diagnosis of monophasic SS was rendered.

The patient underwent a low anterior resection approximately 6 weeks after diagnosis. On gross examination, there was a $6.3 \times 4.1 \times 4.0$ cm fungating tan-brown tumor with focal areas of hemorrhage. Microscopic examination showed more classic morphologic features of monophasic SS than the biopsy: the tumor involved the mucosa, submucosa (*Figure 1a*), and muscularis propria and extended into the perirectal adipose tissue. Spindled to ovoid cells with hyper- and hypocellular areas were seen, admixed with dilated staghorn vessels and abundant mitotic figures (*Figure 1b–1d*). The resection margins were negative for tumor. Perineural invasion was not identified. Lymph node metastasis was present in 4 out of 18 lymph nodes.

Shortly after the resection, multiple liver metastases were detected by radiographic imaging. The patient later developed abdominal and peritoneal sarcomatosis, ascites, as well as a new pelvic mass. She underwent chemotherapy (which included doxorubicin, ifosamide, gemcitabine, and docetaxel); however, she continued to have persistent disease refractory to treatment. Ultimately, she elected to pursue

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Table 1. Summary of primary synovial sarcoma arising from esophagus, stomach, and intestine

Author, year	Age (years)	Gender	Site	Size (cm)	Type	Prognosis (months)
Palmer, 1983	75	F	Upper and middle esophagus	2.5	~	Dead of disease (24)
Amr, 1984	25	M	Upper esophagus	5	Biphasic	No recurrence (36)
Bloch, 1987	15	M	Upper esophagus	10	Biphasic	Free of disease (36)
Caldwell, 1991	29	F	Upper esophagus	~	~	Free of disease (195)
Anton-Pacheco, 1996	14	F	Upper esophagus	7	Biphasic	Tumor in cervical node (10)
Habu, 1998	20	M	Upper esophagus	7.7	Biphasic	No recurrence (20)
Bonavina, 1998	63	F	Lower esophagus	5	Biphasic	Recurrence (13)
Nakhjavani, 1999	15	F	Upper esophagus	3	~	Alive (53)
Billings, 2000	70	M	Cervical esophagus	7	Biphasic	Dead of disease (42)
Butori, 2006	72	F	Middle esophagus	11	Biphasic and poorly differentiated	No recurrence (6)
Niihara, 2015	28	M	Upper and mid esophagus	10	Biphasic and poorly differentiated	~
Doroudinia, 2017	47	M	GEJ	5.2	Biphasic	No recurrence (21)
Sasaki, 2020	47	F	Cervical esophagus	5.2	Monophasic	No recurrence (81)
Garcia-Rodriguez, 2019	54	F	Upper esophagus	7.8	~	Recent case
Billings, 2000	55	F	Distal stomach	16	Biphasic and poorly differentiated	Dead of disease (6)
Akhunji, 2007	42	M	Posterior gastric wall	11.5	Biphasic	Dead (24)
Makhlouf, 2008	67	F	Body antrum junction	0.8	Monophasic	No recurrence (12)
Makhlouf, 2008	49	M	Body of stomach	2	Monophasic and poorly differentiated	Dead of disease (29)
Makhlouf, 2008	68	F	Body of stomach	2	Monophasic	No recurrence (22)
Makhlouf, 2008	29	M	Body of stomach	2.8	Monophasic	No recurrence (224)
Makhlouf, 2008	54	F	Antrum, gastroduodenal junction	3	Monophasic	~
Makhlouf, 2008	58	F	Lesser curvature/body	3	Monophasic	No recurrence (21)
Makhlouf, 2008	37	F	Fundus	4	Monophasic	Dead of other disease (48)
Makhlouf, 2008	50	M	Distal fundus	6	Monophasic	Alive with recurrence (6)
Makhlouf, 2008	42	M	Greater curvature/body	8	Biphasic	Dead of disease (25)
Makhlouf, 2008	66	F	Fundus	15	Monophasic	~
Wang, 2012	38	F	Mid portion of gastric body	7.2	Monophasic	Alive with disease (6)
Sinniah, 2012	44	F	Proximal lesser curve stomach	4.7	Monophasic	No recurrence (60)
Kamata, 2013	42	F	Body of stomach	3.5	Monophasic	No recurrence (72)
Sahara, 2013	22	F	Mid gastric body	2.5	Monophasic	~
Michot, 2014	62	M	Cardia and fundus	3.8	Monophasic	No recurrence (9)
Torres Rivas, 2014	44	M	Lesser curvature	15	Monophasic	~
Wong, 2015	49	F	Stomach	3.5	Monophasic	No recurrence (10)
Wong, 2015	35	F	Stomach	12	Monophasic	Liver metastases (24)
Romeo, 2015	50	F	Gastric body	8	Monophasic	Lost to follow-up
Romeo, 2015	36	M	Gastric	6	Poorly differentiated	Alive with disease (36)
Romeo, 2015	37	M	Gastric	2	Monophasic	Recent case
Romeo, 2015	26	M	Gastric	~	Monophasic	Alive with disease (185)
Romeo, 2015	58	M	Gastric	10	Monophasic	Dead of disease (6)

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Table 1. Continued

Author, year	Age (years)	Gender	Site	Size (cm)	Type	Prognosis (months)
Romeo, 2015	21	M	Gastric	10	Monophasic	Lost (48)
Romeo, 2015	36	M	Gastric	6	Biphasic	Lost (12)
Romeo, 2015	54	F	Gastric	3.8	Monophasic	Recent case
So, 2017	51	F	Mid body of stomach	0.9	Monophasic	No recurrence (2)
Ogino, 2018	27	F	Lower stomach	2	~	Free of disease (6)
Olsen, 2018	57	F	Gastric body	1.8	Monophasic	~
Hu, 2019	58	M	Gastric body	6.3	Monophasic	Peritoneal metastasis (2.5)
Fuente, 2019	42	M	Lesser curvature	3	Monophasic	No recurrence (12)
Manohar, 2021	13	M	Body and fundus	11	Monophasic	Free of disease (6)
Wong, 2020	54	M	Lesser curvature	1.6	Monophasic	No recurrence (18)
Krupinska, 2020	48	F	Body and pylorus	9	Monophasic	Recent case
Chan, 2004	28	M	Proximal jejunum	15	Monophasic	Dead (1)
Parfitt, 2007	32	M	Sigmoid colon	2	Monophasic	Free of disease (5)
Schreiber-Facklam, 2007	39	F	Distal duodenum	5	Monophasic	Local recurrence (8)
Company-Campins, 2009	69	F	First portion of duodenum	8	Monophasic	Dead (1)
Garcia-Ruiz, 2010	70	M	Third portion of duodenum	9	Biphasic	~
Eriksen, 2010	39	F	Mid ileum	4.5	Monophasic	Free of disease (24)
Alsharief, 2012	29	F	Terminal ileum	8	Monophasic	Free of disease (24)
Hostetter, 2012	~	F	Rectum	5.2	Monophasic	~
Sista, 2015	56	M	Ileum	7.9	Monophasic	~
Romeo, 2015	49	M	Ileum	8	Monophasic	Dead of disease (60)
Romeo, 2015	40	M	Colon	5.5	Monophasic	Free of disease (132)
Romeo, 2015	44	F	Rectosigmoid colon	6.3	Poorly differentiated	Dead of disease (47)
Romeo, 2015	44	F	Rectosigmoid colon	6.3	Poorly differentiated	Dead of disease (47)
Romeo, 2015	17	M	Ileum/colon	7.5	Monophasic	Free of disease (108)
Eid, 2017	10	M	Left colon under flexure	4	Monophasic	Free of disease (72)
Lee, 2018	50	F	Mid transverse colon	9.3	Biphasic	~
Ioannidis, 2019	54	M	Sigmoid colon	20	Monophasic	~
Current case	48	F	Rectum	6.3	Monophasic	Dead of disease (48)

~ indicates data not provided; GEJ, gastroesophageal junction.

hospice care. The time from date of diagnosis to date of death was almost 4 years.

DISCUSSION

Together, 68 cases (including the current case) of primary SS arising from the esophagus ($n = 14$), stomach ($n = 36$), and intestine ($n = 18$) have been reported (Table 1). The mean age was 43.5 years (range, 10–75 years), with 32 men and 36 women. The mean tumor size was 6.5 cm (range, 0.8–20 cm); 44 cases were monophasic, 12 were biphasic, 7 were poorly differentiated, and 5 were unclassified. The

survival time of 50 reported cases varied from 1 month to 224 months (18 cases did not report survival time).

For our statistical analysis, 50 cases with reported follow-up outcomes were divided into three groups: deceased, alive with disease, and alive without disease. One-way ANOVA and the post hoc Bonferroni test (when applicable) as well as multivariable Cox proportional hazard regression model were applied to risk factors of age and tumor size. Fisher's exact test was applied to risk factors of gender and tumor type. A P value <0.05 was considered statistically significant. No significant differences were found by the risk factor of

age ($P = 0.08$), gender ($P = 0.97$), or tumor type ($P = 0.29$). Tumor size was significantly higher in the deceased group compared to the alive without disease group ($P < 0.05$).

Further analysis of all 68 cases by multivariable Cox proportional hazard regression model showed a linear relationship between hazard of mortality and age, and a nonlinear relationship between hazard of mortality and tumor size. Risk of mortality increased significantly with increasing age (Figure 2a, hazard ratio = 1.073, $P = 0.0009$). Interestingly, risk of mortality increased almost linearly when tumor size was ≥ 5 cm (Figure 2b, hazard ratio = 1.46, $P = 0.003$); however, the risk showed a nonsignificantly decreased trend

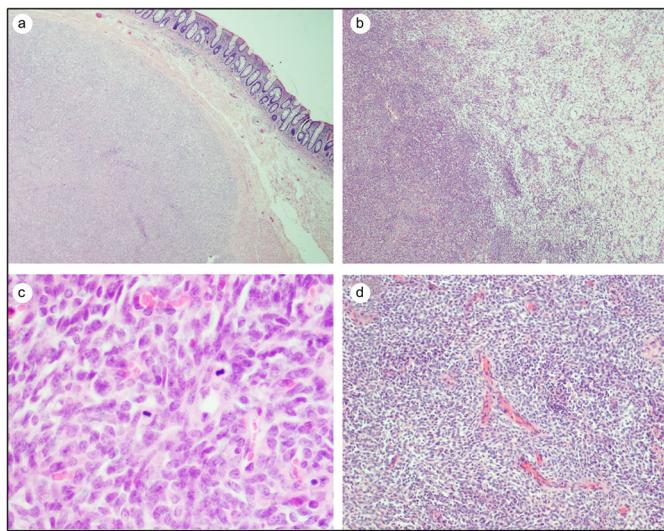


Figure 1. Histology of synovial sarcoma in the rectum. (a) Tumor involves colonic submucosa. (b) Low-power view of hypercellular and hypocellular tumor areas. (c) Abundant mitotic figures in the tumor cells. (d) Dilated staghorn vessels admixed with tumor cells.

when the tumor size was <5 cm (Figure 2b, hazard ratio = 0.4, $P = 0.4$).

Our review and analysis of SS in the esophagus, stomach, and intestine revealed that patients with aging or a large tumor size (≥ 5 cm) have a higher risk of rapidly progressing to death. We recommend that SS be considered in the differential for any spindle cell lesion in the digestive tract.

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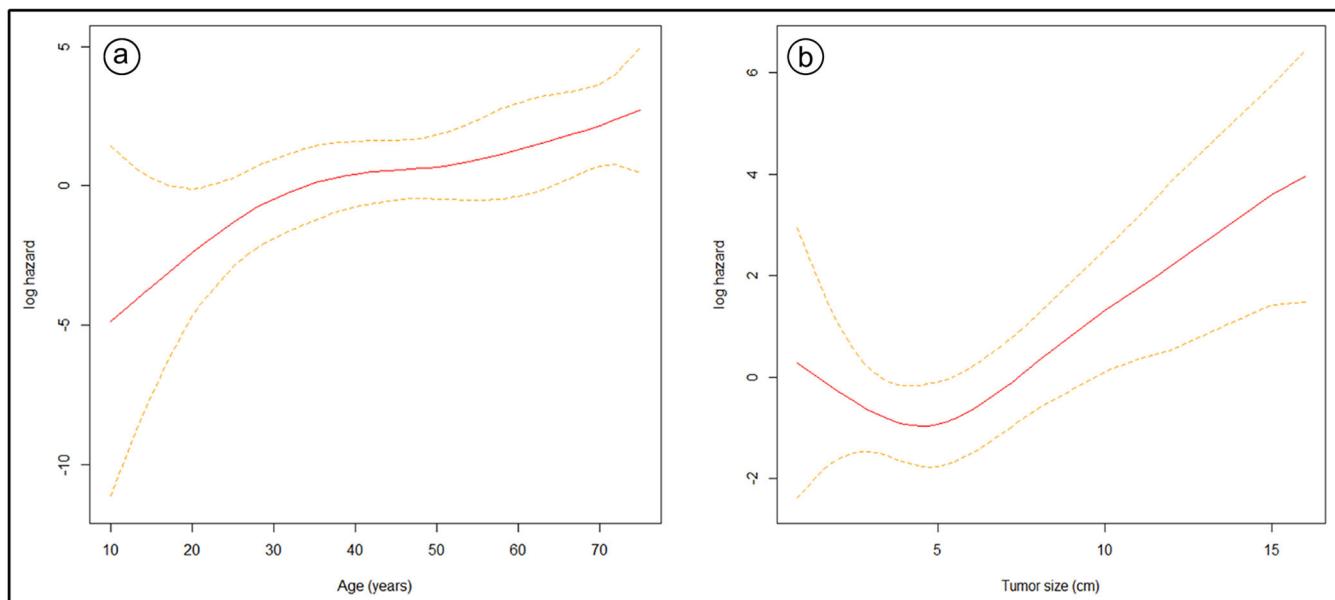


Figure 2. Multivariable Cox proportional hazard regression model. (a) Risk of mortality increased significantly with increasing age. (b) Risk of mortality increased almost linearly when tumor size was ≥ 5 cm, but risk of mortality showed a nonsignificantly decreased trend when tumor size was <5 cm.

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